



Agent Orange Brief

Prepared by the Environmental Agents Service (131)

D3

VA Central Office, Washington, DC 20420

Jan 2001

AGENT ORANGE AND NON-HODGKIN'S LYMPHOMA

What are non-Hodgkin's lymphomas?

The term "non-Hodgkin's lymphoma" is used to describe a group of malignant tumors that affect the lymph glands and other lymphatic tissue. These tumors are relatively rare (about 3% of all cancers that occur among the U.S. general population), and although survival has improved during the past 20 years, these diseases tend to be fatal.

What prompted initial concerns among Vietnam veterans about non-Hodgkin's lymphomas?

The possibility that exposure to phenoxy herbicides such as Agent Orange may have caused rare forms of cancer in humans was suggested in Swedish studies published in 1979 and 1981. Investigations in Sweden reported a six-fold increased risk of malignant lymphomas (Hodgkin's disease and non-Hodgkin's lymphomas combined) among persons occupationally exposed to phenoxy herbicides or chlorophenols compared to persons without exposure.

Have more recent results supported or conflicted with these Swedish studies?

An analysis using the New Zealand Cancer registry indicated an elevated risk of malignant lymphomas (including non-Hodgkin's lymphomas, Hodgkin's disease, and multiple myeloma) linked with agricultural occupations; however, further analyses restricted to interviews of non-Hodgkin's lymphoma and control subjects found no significant differences between non-Hodgkin's lymphoma cases and controls regarding their potential exposure to phenoxy herbicides or chlorophenols.

A population-based study in Kansas found a 6-fold excess risk of non-Hodgkin's lymphomas among farmers exposed to herbicides more than 20 days per year (regardless of the number of years of herbicide use) compared to non-farmers. Excess risk of non-Hodgkin's lymphomas in Kansas was associated primarily with long-term use of the herbicide 2,4-D, one of the ingredients of Agent Orange. (This was not the ingredient of Agent Orange, which contained TCDD or dioxin, which has caused a variety of illnesses in laboratory animals.) Hodgkin's disease was not associated with herbicide use in Kansas.

A study in Washington State demonstrated small but significantly increased risks of developing non-Hodgkin's lymphomas in association with some occupational activities where phenoxy herbicides have been used in combination with other types of chemicals, particularly for long periods. The study results did not demonstrate an association between increased cancer risks and exposure to any specific phenoxy herbicide product alone.

A 1987 study of Swedish pesticide applicators, 72% of who were exposed also to phenoxy herbicides, found no excess risk of non-Hodgkin's lymphomas or Hodgkin's Disease.

Conflicting results have also been seen in studies of Vietnam veterans. No significant excess mortality from non-Hodgkin's lymphomas was reported among New York State Vietnam veterans, Australian Vietnam veterans, U.S. Vietnam veterans in the Centers for Disease Control (CDC) Vietnam Experience Study or among Air Force "Ranch Hands" who handled and sprayed herbicides in Vietnam. West Virginia Vietnam veterans had an excess of deaths from all lymphomas compared to non-Vietnam veterans. In a mortality study of U.S. Army and Marine Corps veterans, a significantly higher than expected proportion of non-Hodgkin's lymphomas occurred among U.S. Marine Vietnam veterans, compared to Marines who did not serve in Vietnam. When Marine Vietnam veterans were compared with all non-Vietnam veterans combined (Army and Marine), there was no excess of non-Hodgkin's lymphoma deaths. Non-Hodgkin's lymphomas were not elevated among Army Vietnam veterans included in the same study. Army veterans who served in the same geographical area (I Corps) as the Marines experienced no excess of deaths due to non-Hodgkin's lymphomas.

The CDC Selected Cancers Study suggested that Vietnam veterans are at increased risk of developing this disease, but the excess was confined to men who served in the "blue-water" Navy. A VA study published in the Journal of Occupational Medicine in July 1991 indicated that military service in Vietnam did not increase the risk of developing non-Hodgkin's lymphomas.

Does VA recognize non-Hodgkin's lymphomas as service-connected for Vietnam veterans?

Yes. On March 29, 1990, Secretary Derwinski announced that VA would service-connect non-Hodgkin's lymphomas based on service in Vietnam. This announcement was prompted by release of results of the CDC Selected Cancers Study, which indicated that Vietnam veterans are at increased risk of developing non-Hodgkin's lymphomas. CDC found no evidence that the increased risk was due to Agent Orange. Final regulations implementing Secretary Derwinski's decision were published in the Federal Register in October 1990. (See 55 Fed. Reg. 43123, October 26, 1990).

What did Public Law 102-4, the Agent Orange Act of 1991, do for Vietnam veterans with non-Hodgkin's lymphoma?

Section 2, Public Law 102-4, enacted February 6, 1991, established by statute the presumption of service connection for certain diseases -

including non-Hodgkin's lymphoma manifested to a degree of 10 percent or more - associated with exposure to certain herbicide agents.

In July 1992, a proposed rule implementing the presumptions established by this law was published in the Federal Register for public comment. (See 57 Fed. Reg. 30707, July 10, 1992). In May 1993, the rule was finalized and published in the Federal Register. (See 58 Fed. Reg. 29107, May 19, 1993).

What did the National Academy of Sciences (NAS) conclude about non-Hodgkin's lymphomas (NHL) in its 1993 report, entitled Veterans and Agent Orange - Health Effects of Herbicides Used in Vietnam?

The 832-page NAS report contained the following statements:

The production studies suggest an increased risk of NHL from exposure to TCDD-contaminated chemicals, but not of a degree that would allow a definitive statement to be made....

Thus, taken as a group, the studies of agricultural and forestry workers suggest that there is an association between exposure to herbicides (including 2,4-D) and NHL....

Although no single (veterans) study shows definite associations between NHL and exposure to herbicides since individual exposures were not determined except for Ranch Hands, none rules out the possibility that an herbicide-related risk of NHL existed for some military personnel during service in Vietnam....

Thus, unlike most of the other cancers studied by the committee for which the data do not distinguish between the effects of herbicides and TCDD, the available epidemiologic data suggest that the phenoxy herbicides, including 2,4-D, rather than TCDD may be associated with non-Hodgkin's lymphomas....

Evidence is sufficient to conclude that there is a positive association between exposure to herbicides (2,4-D; 2,4,5-T and its contaminant TCDD; cacodylic acid; and picloram) and non-Hodgkin's lymphoma.

What did the NAS conclude about non-Hodgkin's lymphomas in its 1996 update?

The NAS indicated that "recent scientific literature continues to support the conclusion that there is a positive association between exposure to herbicides and non-Hodgkin's lymphoma."

What did the NAS conclude about non-Hodgkin's lymphomas in its 1998 update?

The NAS report stated, "Evidence continues to accumulate to conclude of a positive association between exposure to the herbicides (considered in this report) and non-Hodgkin's lymphoma. The strength of the evidence

regarding association is drawn from occupational and other studies in which subjects were exposed to a variety of herbicides and herbicide components and is increasing in significance, including among studies of Vietnam veterans."

Where can a veteran get additional information regarding non-Hodgkin's lymphomas?

Information on non-Hodgkin's lymphomas and related matters can be obtained at VA medical center libraries, from the Registry Physician at VA medical centers, or from the Environmental Agents Service (131), Department of Veterans Affairs, 810 Vermont Avenue, N.W., Washington, DC 20420.